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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/520,771 | 12/05/2005 | Mohammad Reza Mehrabi | 22508-001 | 9945 |

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| EXAMINER | |
|---|---|
| THOMAS, TIMOTHY P | |
| ART UNIT | PAPER NUMBER |
| 1628 | |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/520,771 | MEHRABI, MOHAMMAD REZA | |
| | Examiner | Art Unit | |
| | TIMOTHY P. THOMAS | 1628 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *05 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *3-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 14-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/5/2009 has been entered.

### *Response to Arguments*

2. Applicants' arguments, filed 10/5/2009, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

3. Applicant's arguments with respect to the rejection of claims 1-2 under 35 USC 102 have been fully considered but they are not persuasive:

Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Virgolini et al. ("Beneficial effect of long-term PCE1-treatment in left ventricular heart failure"; 1989; Prostaglandins, Leukotrienes, and Essential Fatty Acids; 38(3): 177-80).

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. Claims 1-2 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Virgolini et al. ("Beneficial effect of long-term PCE1-treatment in left ventricular heart failure"; 1989; Prostaglandins, Leukotrienes, and Essential Fatty Acids; 38(3): 177-80; cited in a prior Office Action).

The rejection basis is of record; additionally, with respect to the claim limitation "wherein the method does not include an incremental dose of 40 ng/kg/min", recited in claim 1, improvement was seen at the rather low doses administered in the range from 10-30 ng/kg/min (abstract); long term responders received a continuous rate of 20 ng/kg/min i.v. continuously; neither of these segments of treatment include an incremental dose of 40 ng/kg/min; therefore, neither of these segments are excluded from anticipating the instant claims.

It is noted that one segment of the preliminary treatment involved increasing dose rates from 10 to 100 ng/kg/min for 10 minutes each. Although the details of which increments were administered do not include a specific amount taught of 40 ng/kg/min, it might be argued that 40 ng/kg/min would have been one of the increments in the 10-

100 range taught. To address this possibility, the "long-term" segment of the treatment does not involve the incremental dose of 40 ng/kg/min; i.e., the long term segment anticipates the claims without the 40 ng/kg/min increment.

It might be argued that the method taught by Virgolini would have necessarily included the preliminary 10-100 range increasing doses that included the 40 ng/kg/min increment, no longer anticipating a claim that specifically excludes this increment. Even if this point of view were adopted, it would have been obvious to administer only the long term dosage of 20 ng/kg/min to an individual with congestive heart failure (without the preliminary 10-100 ng/kg/min incremental increase), motivated by the teaching of Virgolini of a significant benefit the 20 ng/kg/min dose provided in this patient population, and because low doses of 10-30 ng/kg/min are taught to provide a benefit of LVEF without affecting blood pressure or heart rate (abstract).

Applicant's arguments do not comply with 37 CFR 1.111(c) because they do not clearly point out the patentable novelty which he or she thinks the claims present in view of the state of the art disclosed by the reference cited. Further, they do not show how the amendments avoid such reference. No mention has been made in applicant's arguments of the rejection under 35 USC 102 as anticipated by Virgolini; therefore they are not compliant with 37 CFR 1.111(c).

7. Applicant's arguments with respect to the rejection of claims 1-2 and 14-15 under 35 USC 103 have been fully considered but they are not persuasive:

Claims 1-2 and 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Stanek et al. ("Dose-effect relationships of prostaglandin E1 in severe endstage

chronic heart failure"; 1997 Jan; Jpn. Heart J.; 38(1): 53-65; cited in a prior Office Action).

With respect to claims 1-2 and 14-15, the rejection is maintained for the reasons of record and the reasons that follow. With respect to the claim limitation "wherein the method does not include an incremental dose of 40 ng/kg/min", recited in claim 1, the Stanek study included subpopulations where the uptitration (from initial dose of 2.5 ng/kg/min) of PGE1 to 5 ng/kg/min was followed by subsequent dose steps of 10, 15, 20, 25 and 30 ng/kg/min, which was tolerated at a maximum tolerated dose (MTD) of 30 ng/kg/min by 10 patients (p. 57, last paragraph, Group A; p. 56, Administration of PGE1 paragraph); the dose increase was stopped upon appearance of intolerable side effects, i.e., the MTD (p. 56; Administration of PGE1 paragraph). An MTD of 30 ng/kg/min meets the MTD criteria of claims 14, 15 and 16 of 29 ± 1 ng/kg/min; these 10 patients with an MTD of 30 ng/kg/min also did not receive an incremental dose of 40 ng/kg/min, satisfying the negative limitation recited in claims 1 and 16. With respect to claim 16, the clinical study involved patients with chronic heart failure (title, abstract) who received the same incremental dosing regimen, meeting the method limitation of this disease and steps recited in claim 16.

Applicant argues that Stanek does not disclose every recited limitation, specifically "wherein the method does not include an incremental dose of 40 ng/kg/min", which is specifically excluded by the instant claims. This is not persuasive. While it is noted that the Stanek clinical trial does involve 40 ng/kg/min increment for some patients that had reached this level without reaching the MTD at a lower amount, the 10

subjects with an MTD of 30 ng/kg/min is an embodiment of the clinical trial where the subjects did not receive a 40 ng/kg/min incremental dose (the dose increment was stopped at 30 ng/kg/min), satisfying the negative limitation of the instant claims. In construing the claims, the method only requires administering to "a [one] subject", not to every individual taking part in a clinical trial or every patient of some patient population; the 10 individuals that received a MTD of 30 ng/kg/min are 10 individual subjects that meet the required claim limitations, anticipating the claims.

Applicant makes some comments regarding how claim interpretation should be interpreted in light of the specification, but it is not clear what meaning these comments have to the way the instant claims are being construed.

Applicant's comments about teaching away, with respect to nonobviousness, are not relevant to an anticipation rejection. Although it is acknowledged that Stanek administered an incremental amount of 40 ng/kg/min to a few individuals that had not reached the MTD by this increment, many other individuals had reached the MTD before 40 ng/kg/min, these individuals did not receive 40 ng/kg/min. For these individuals, the negative claim limitation is satisfied. It is noted that MPEP 2141.02 and 2143.01 both refer to the subject of obviousness, and to rejections made under 35 USC 103; these sections are not applicable to the instant rejection basis, under 35 USC 102. Similarly, the argument of proceeding contrary to accepted wisdom in the art being evidence of nonobviousness, is not applicable to anticipation.

***Claim Rejections - 35 USC § 112***

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-2 and 14-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The phrases "wherein the method does not include an incremental dose of 40 ng/kg/min" in claim 1, and wherein the increasing step does not provide an incremental dose of 40 mg/kg/min" in claim 16 are New Matter, not described in the written description as originally filed. The specific amount of 40 mg/kg/min is not specifically recited, either positively or negatively; therefore the exclusion of this specific amount does not have description to demonstrate applicant was in possession of this embodiment, or to place the public in possession of this exclusion, at the time of filing.

***Conclusion***

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY P. THOMAS whose telephone number is (571)272-8994. The examiner can normally be reached on Monday-Thursday 6:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on (571) 272-2919. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Timothy P Thomas/
Examiner, Art Unit 1628